DEVELOPMENT AND EVALUATION OF FLOATING TABLETS BEARING MODEL ANTIULCER DRUG FOR THE TREATMENT OF PEPTIC ULCER

A synopsis submitted

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By
Pranjal Kumar Singh

Under the supervision of

(Prof.) Dr. T. S. Easwari
Professor
IIMT College of Medical Sciences

IIMT UNIVERSITY, MEERUT
UTTAR PRADESH, 250001

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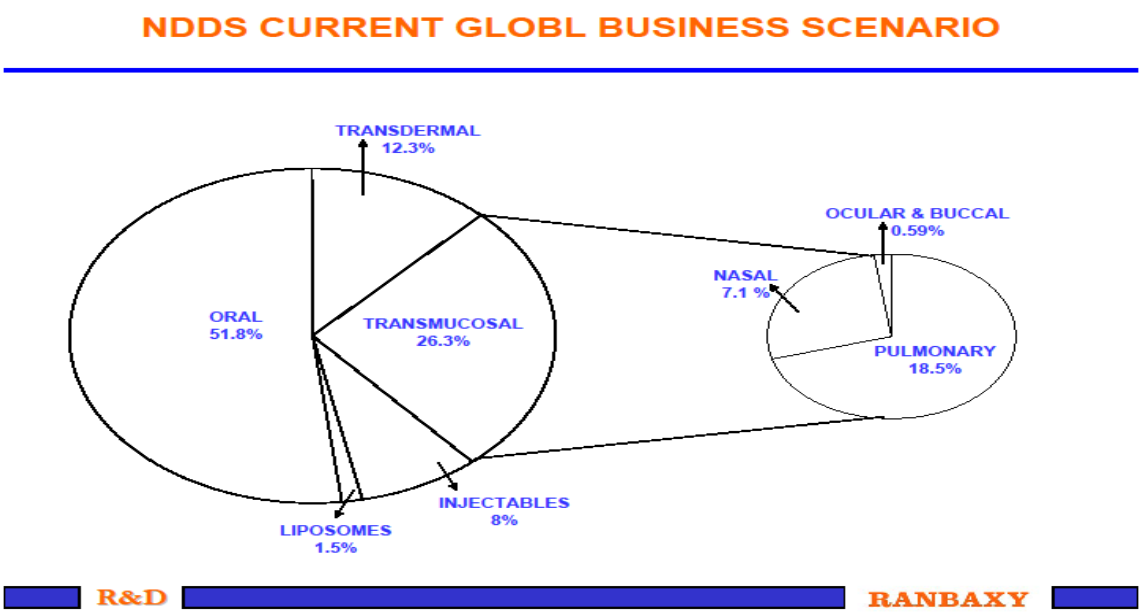
INTRODUCTION

NEW DRUGS DELIVERY SYSTEM

innovative Drug Delivery System: A number of technical developments in drug delivery have led to the creation of brand-new or innovative drug delivery systems. There are advantages and disadvantages to each of these approaches, but they can be used to control the dosage, extend the duration of an agent's therapeutic effect, or direct it to a specific organ or tissue.



Need for gastro-retentive drug delivery

Drugs are especially interested in a regulated drug transport system with an extended stomach residence period.

1. Which are specifically effective against Helicobacter pylori in the stomach, such as misoprostol, antacids, and antibiotics.

2. Drugs with an upper small intestine or stomach absorption window, such as riboflavin, furosemide, paminobenzoic acid, and L-DOPA

Approaches for gastro-retention

Several different forms of gastroretentive drug delivery systems can do this.

1. System that floats
2. System that swells and expands
3. Bioadhesive technology
4. Modified shape system

HISTORY & DISCRIPTION

As early as 1962, the idea of a floating medication delivery device was discussed in the literature.

While floating on stomach contents, the drug is progressively removed. The medicine empties the stomach. As a result, the duration of gastric retention is extended, and changes in plasma drug concentration are better managed.

One challenge is limiting dose form in the desired gastrointestinal region. The process of drug uptake from the digestive system is intricate and influenced by a variety of factors. It is commonly accepted that the length of time a medicine spends in touch with the small intestine mucosa influences how much of the gastrointestinal tract it absorbs3. The brief intestinal transit time is critical for partially absorbed medicines.

Gastroretentive mechanisms can keep drugs in the stomach for hours. Prolonged stomach retention improves bioavailability, solubility, and drug waste for high-pH medicines. It can deliver drugs to the abdomen and small intestines. Gastro retention makes newer medications with new therapeutic options and patient benefits more accessible.

Basic Gastrointestinal Physiology

Figure No.1

Fasting and eating empty the stomach. Both states' motility patterns differ. The stomach and intestine undergo interdigestive electrical processes every two to three hours while fasting. Wilson and Washington5 divide the interdigestive and migrating myloelectric cycles (MMC) into four phases.

Phase I Rare contractions last 40–60 minutes.

Phase II involves intermittent contractions and action potentials lasting 40–60 minutes. Frequency and intensity increase during the phase.

Phase III the blast phase—takes four to six minutes. It has frequent, forceful contractions. This wave moves all undigested material. Housekeeping wave is another term.

Phase IV lasts 0–5 minutes between cycles III and I. A mixed meal changes contractions from fasting to nourished. This digestive motility pattern contracts constantly in phase II of fasting 6.

Gastric Retention Causes and Effects

Oral dosage form gastrointestinal retention depends on several factors. To cross the pyloric valve and enter the small intestine, particles must be 1–2 mm7. Fasting stomach pH is 1.5–2.0; fed stomach pH is 2.0–6.0. Water consumption raises stomach pH to 6.0 to 9.0. Basic drugs dissolve better when fed than when fasted because the liquid quickly empties the stomach, preventing the stomach from creating adequate acid.

Meals' viscosity, volume, and calories affect stomach emptying speed. Dietary density affects stomach emptying. If the meal has the same number of calories, it doesn't matter if it's high in protein, fat, or carbs. Acidity and calories delay stomach emptying. Age, gender, BMI, posture, and pathologies (diabetes, Chron's disease) affect gastric emptying. Aging people have a slower rate of stomach emptying. In general, females empty their stomachs more slowly than males. Depression slows down gastric emptying rates whereas stress speeds them up8.

Resting stomach volume is 25–50 mL. Liquid intake affects stomach emptying. High volumes empty quickly. Body-temperature drinks move through the stomach faster. Studies show that dose form size affects stomach emptying speed. Smaller pills leave the stomach during digestion, but larger pills leave during housekeeping waves.

CLASSIFICATION

Non-effervescent FDDS:

- The medicine is tightly mixed with a hydrocolloid that gels in stomach fluid following oral administration to create floating dosage forms. The outer gelatinous barrier protects this hydrocolloid's structure and bulk density. The air-filled polymer makes these dosage forms float.
- Sheth and Tossounian suggested that the hydrocolloid first forms a gel at the dosage form's surface when it interacts with an aqueous solution. Gel structure controls solvent and drug diffusion into and out of the dosage form.

Effervescent FDDS:

- The matrices are designed to release carbon dioxide from the stomach's acidity into the gellified hydrocolloid. The dosage form rises and swims on chyme.
- Stockwell et al. produced floating capsules from sodium alginate and sodium bicarbonate. The devices floated in vitro because the moisturizing gel network produced CO2 when exposed to acidic conditions.
- Carbonates provide buoyancy and the alkaline environment polymers need to gel. For bioadhesive hydrogel formation, CO2 release accelerates floating tablet hydration.
- Floating dosage forms with an in-situ gas-producing technology should float higher and release drugs better. Since drug release optimization might vary buoyancy, formulation optimization may necessitate independent buoyancy management.
- Gerogiannis and colleagues investigated the floating and swelling properties of common excipients. Thus, higher molecular weight and fewer hydrophilic polymers improve floating qualities.

ADVANTAGES

- Sustained drug delivery: As was already indicated, the low GRT available for absorption frequently restricts the amount of medication that may be absorbed from oral controlled release (CR) dose forms.
- Drug delivery at a precise location.
- A potential strategy is to use a floating dose form, particularly for medications with few upper small intestine absorption sites.
- The stomach receives the medicine gradually. This reduces the drug's blood-circulation effects. Due to extended gastrointestinal availability, site-directed administration devices may reduce dosage frequency.
- Helicobacter pylori removal calls for the repeated administration of several medications, which frequently leads to low patient compliance. By employing GRDDS, more dependable therapy may be accomplished. Amoxycillin trihydrate has been released gradually using floating alginate beads.

PROBLEM STATEMENT

Two basic problems may come that has to be encountered, that are –

1. Flotation of dosage form in the case of sustained release for several hours.
2. Bioadhesion in peptic ulcer.

OBJECTIVE OF THE STUDY

The current study created a bilayer floating-bioadhesive drug delivery system for a model pharmaceutical that combined flotation and bioadhesion to extend stomach residency. In order to release all the medication in the required period, a controlled drug delivery system must extend the dose form's duration in the GIT. The hydrodynamically balanced system, or FDDS, increases medication bioavailability by lengthening stomach residence time. Thus, FDDS float in the stomach without impeding stomach emptying. The system slowly releases the drug while floating on stomach contents.

Rationale for selection of gastro- retentive drug delivery system:

- Reduce dose frequency to increase patient compliance.
- Achieved is site-specific medication delivery.
- thanks to continuous release, stomach discomfort is avoided.
- to ensure the stomach's long-term medication availability.
- to increase therapeutic effectiveness.
- to more quickly treat or manage diseases.

FORMULATION HYPOTHESIS

It will have two layers: a mucoadhesive layer and a floating layer with sustained release. All components were combined in the pestle and mortar after being filtered through a 60# sieve. The produced floating layer granules will be combined with eight quantities of the mildly compressed sustained release layer. In a single station rotary press tablet machine, weight granules of the mucoadhesive layer were combined with the compressed floating sustained release layer.

REVIEW OF LITERATURE

1. Timmermans and Andre found that floating units stayed buoyant in stomach secretions.

2. Ozdemir et al. created furosemide-controlled release floating bilayer tablets.Shorter compression forces started floating faster in in vitro studies. When crushed at 15 MPa, the tablets floated after 20 minutes, but at 32 MPa, it took 45 minutes.

3. Choi et al. floated alginate beads with calcium carbonate and sodium bicarbonate to study how CO2 generation affects materials' physical properties, shape, and release rates.

4. Li et al. explore how formulation parameters affect gastro floating drug delivery system floating characteristics. Higher HPMC/carbopol ratios improved floating, indicating carbopol hinders floating.

5. Penners et al. created an expandable tablet that immediately swell in water. Gases were added. As gas was generated, the system's density reduced, making it float atop stomach contents.

6. Fassihi and Yang created a tablet having one drug layer and at least two barrier layers. The pill's protective layers broke down, exposing more medicine. A gas-evolving agent on one barrier layer made the tablet float.

7. Talwar et al. produced a once-daily oral ciprofloxacin formulation. The moist gel matrix complicated medicine diffusion, prolonging its release.

8. Baumgartner et al. created a matrix-floating tablet. Fasting beagle dogs showed extended stomach residence in in vivo experiments. Since stomach emptying and gastric motility were similar in humans and dogs.

9. Moursy et al. produced continuous-release nicardipine hydrochloride floating capsules. In vitro research compared 20-mg MICARD nicardipine HCl. Hydrocolloid increased floating. Sodium bicarbonate added buoyancy. After distribution, sustained release capsules lasted longer.

10. Atyabi and colleagues devised a floating system. A semipermeable membrane was wrapped around loaded beads to slow CO2 loss. Gamma radio scintigraphy was used to observe coated

and uncoated beads in vivo with 12 healthy human subjects. Studies found that coated beads spent 24 hours in the stomach, compared to 1–3 hours for untreated beads.

11. Thanoo et al. solvent-evaporated polycarbonate microspheres. SEM demonstrated that polycarbonate in dichloromethane. High-drug-loaded microspheres floated on stomach and intestinal fluids.

12. Nur-Zhang Carbopol 934P and HPMC (4000 and 15000 cps) made captopril floating tablets. The tablet's buoyancy comes from internal cavities (porosity) and stomach secretions inflating hydrocolloid particles on its surface. Floating captopril tablets released captopril for 24 hours, longer than conventional tablets.

13. Bulgarelli et al. examined how emulsification extraction casein gelatin beads affected matrix composition and process parameters. In both high and low porous matrices, casein increases drug loading.

14. Fell et al. made floating amoxycillin-infused alginate beads. Dropping alginate into a calcium chloride solution, extracting the gel beads, and freezing the mixture produced the beads. Drug-loaded beads floated for 20 hours at high levels.

15. Streubel et al. developed matrix-forming polymer and powdered polypropylene foam single-unit floating tablets.

RESEARCH METHODOLOGY

The current work will be completed along these lines:

1. Comprehensive literature review

2. Buying pharmaceuticals, chemicals, and other excipients

3. Preformulation research

a) Identification and characterization of drug

b) Drug excipients interaction studies.

1) FT-IR.

4. Floating tablets preparation of gatifloxacin.

Direct compression method.

5. Evaluation and characterization of floating tablets.

a) Thickness,

b) Uniformity of weight,

c) Moisture content,

d) Hardness,

e) Friability,

f) Disintegration,

g) Drug content uniformity,

h) Dissolution.

6. Result and discussion.

EXPECTED CONTRIBUTION OF STUDY

A number of medications have emerged as viable treatments for Peptic ulcer, which can result in duodenal ulcers and a number of cytotoxic side effects. H. pylori is mostly found in the stomach, more especially in the mucous layer subregion. In order to completely remove the infection, extended and continuous medication concentration at that specific spot is required. This results in the creation of sustain-release dose forms for a variety of medications that are therapeutically acceptable.

The goal of this work is to create a novel long-lasting release tablet with a special blend of bioadhesion and floatation to extend the formulation's time in the stomach before absorption while its ability to dissolve reduces with rising pH levels within the physiological range. The development of improved bilayer with floating-bioadhesive dosage forms that demonstrate a special blend of flotation and adhesion for longer residence in the stomach is effectively offered in this work.

Both the demonstration of the model drug's release from the tablets and the evaluation of the impact of various excipients, including hydroxypropyl methylcellulose, will be done.

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